Allergy Abstracts

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From the Allergy Division of
The Jewish Hospital of Brooklyn

Volume 19, Number 3 May, 1954

Asthma and Hay Fever

Effect of Cortisone and Corticotropin on Allergic Reactions. Irwin, J. W., and Burrage, W. S.: Postgrad. Med. **14**: 262, 1953.

The authors review some of their experimental and clinical experiences with cortisone and corticotropin in allergic diseases. No significant differences in the size of reaction at the passive transfer sites were noted when blood was taken prior to or after the administration of corticotropin to the donor. Studies were conducted on the blood vessels of the bulbar conjunctiva by means of a stereoscopic microscope, according to the method of Kinsley and associates. These tests were performed on asthmatic patients during and after cortisone therapy. It was found that the arterioles became constricted, the venules became dilated, and the red blood cells formed aggregates, which were more predominant on the venous side during cortisone therapy.

Children past 6 years of age with asthma which was refractory to the usual forms of therapy were treated with cortisone. Dosage consisted of 50 mg. every 6 hours for the first 24 hours and then 25 mg. every 6 hours until the symptoms subsided. Children with pollen asthma experienced relief on 12.5 to 25 mg. every 12 hours throughout the season. Fourteen adult patients

with intractable asthma of unestablished etiology were kept symptom-free on maintenance doses of cortisone from 1 to 2 years. In drug reactions of the severe anaphylactoid type cortisone or corticotropin were of little value. Short courses of cortisone or corticotropin, however, were beneficial in alleviating the classical delayed symptoms of either drug or serum sickness. It was concluded that allergic investigation, removal of offending allergens, and hyposensitization therapy should be attempted before hormone therapy is instituted. E. W.

Dermatology

Contact Dermatitis From Rubber Caused by Allergic Sensitivity to Thio-Beta-Naphthol. Schamberg, I. L., and Flesch, P.: J. Invest. Dermat. **21**: 59, 1953.

A patient reacted with erythema and vesicle formation following the application of a rubber tourniquet for an interval as brief as 15 seconds. The allergenic factor was identified as the peptizing agent thio-beta-naphthol. As little as 25 micrograms of the pure chemical produced a positive patch reaction. The allergenic agent manifested a high degree of specificity in that patch tests with many closely related compounds gave negative results. M. Cohen.

Treatment of Allergic Diseases With Colchicoside, a New Derivative of Colchicum. Mugler, A., Mantz, J. M., and Murgraff, M. A.: Presse méd. **61**: 1121, 1953.

Four patients with severe acute allergic erythemato-edematous skin reactions, one with a severe generalized serum sickness and one with a local serum reaction, were treated with Colchicoside. The drug was administered intravenously in doses of 6 to 10 mg., once or twice daily for from 2 to 7 days. The pruritus subsided rapidly and somewhat later the redness and swelling disappeared. The patients slept well after the first dose although the drug is not a hypnotic. There were no ill effects from several hundred injections of this drug. I. Glazer.

Cutaneous Sensitization to PAS (an Alarming Reaction After Injection of the Same Product). Tzanck, A., and Sidi, E.: Bull, et mém. Soc. méd. hôp. Paris **68**: 421, 1952.

A woman working in a laboratory manufacturing pharmaceutical products developed a dermatitis of her hands and face. The rash decreased whenever she stopped working. Epicutaneous tests revealed a marked reaction to PAS. When the patient was given a single oral dose of 0.25 Gm. PAS the rash reappeared, the sites flared up, and a general alarming and febrile reaction occurred. I. Glazer.

A Chemical Measure of the Effect of Soaps and Detergents on the Skin. Van Scott, E. J., and Lyon, J. B.: J. Invest. Dermat. **21**: 199, 1953.

Measured amounts of keratin, obtained from stratum corneum, nails, or hair, were incubated in 1 per cent solutions of various soaps and detergents. This concentration was considered to approximate that present on the surface of the skin under conditions of average household contact. After 2 hours of incubation at 40° C., each solution was analyzed for its sulfhydryl content. The amounts of sulfhydryl groups found in these solutions exceeded those of the control solutions, indicating a denaturing effect of soaps and detergents

on the keratin molecule. Since the pH of the solutions was slightly acid, no alkaline dissolving effect on keratin was present.

There was considerable differences in the amounts of sulfhydryl groups liberated by various substances. For example, Phisoderm showed no increase over tap water in its action on human hair and nails. Fab liberated approximately 20 times more sulfhydryl groups in hair and 150 times more sulfhydryl groups in nails than did water.

No clinical correlation between the extent of the denaturing effect and the ability to produce dermatitis by a soap or detergent was made. However, it was suggested that the alteration of the molecular structure of keratin may be an important mechanism in the production of contact dermatitis by these agents. M. Cohen.

The Relation of Eczema to Attitude and to Vascular Reactions of the Human Skin. Graham, D. T., and Wolf, S.: J. Lab. & Clin. Med. **42**: 238, 1953.

Thirty-one patients with eczema ranging in age from 17 to 75 years were studied to determine the relationship between stressful life situations and exacerbations of the disease. Detailed histories elicited a definite correlation between significant events and the onset or exacerbations of the eczema. The relationship of flare-ups and exposure to foods and other allergens was carefully analyzed. Experimental interviews were conducted during which topics known to have been associated with exacerbations of the disease were deliberately introduced. During these interviews, two tests of cutaneous vascular function were performed. One test consisted of the measurement of skin temperature by the Hardy radiometer which reflected the contracted state of the arterioles. In the second tests the tone of the capillaries and venules was estimated by the reactive hyperemia threshold according to the method of Di Palma, Reynolds, and Foster. It was found that exacerbations of eczema occurred in response to frustrating situations where the subject felt that he was restrained from doing as he wished. Dilatation of arterioles, capillaries, and venules was an important factor in the pathogenesis of the disease and was associated with intense itching. It was suggested that actual lesions result from scratching areas of vaodilatation out of proportion to the degree of itching. These patients feel guilty and resort to self-punishment rather than adjusting to their environments. E. W.

Diphenmethanil (Prantal) Methylsulfate. A New Approach in the Treatment of Poison Ivy Dermatitis. Parish, F. A.: Ann. Allergy **11**: 580, 1953.

Diphenmethanil methylsulfate (Prantal), a synthetic anticholinergic medication which is effective in relieving pruritus, was employed in the treatment of 73 unselected patients with poison ivy dermatitis. Topical medications were not used. Relief from pruritus was noted as early as 8 to 12 hours following the institution of therapy and a diminution in weeping was noted within 24 hours. Complete drying was observed in 48 to 72 hours. The lesions disappeared in about 5 days. The usual dose of 100 mg. four times a day for adults and 50 mg. three times a day for children was well tolerated. F.

Effect of Epinephrine Ointment on the Scratched Human Skin. Ames, E. A.: Ann. Allergy **11**: 594, 1953.

Stabilized epinephrine ointment produces blanching when applied to skin scarified to a fairly consistent depth with a Morrison scratcher. It was found that the size of the blanched area and the duration of blanching varied di-

rectly with the rapidity of the onset of blanching, i.e., the more rapid the onset after application of the ointment, the larger was the area involved and the longer the duration of action. Although there was little difference in the effect of 1:500 and 1:1,000 dilutions, greater dilutions delayed the time of onset with a resultant decrease in the area involved and a diminution in the duration of the blanching. When the depth of the scratches was increased, a more rapid onset in blanching occurred, but if there was bleeding of any consequence the blanching effect of the ointment was nullified. F.

The Effect of Hydrocortisone Acetate Ointment on Pruritus Ani. Alexander, R. M., and Manheim, S. D.: J. Invest. Dermat. **21**: 223, 1953.

A group of patients with severe intractable pruritus ani was treated with 2.5 per cent hydrocortisone acetate ointment. The ointment was applied to the affected area 2 or 3 times daily in small amounts. Of 29 patients treated from 2 to 5 months, all except 3 had excellent results. Symptoms tended to disappear after one week of therapy and the skin became normal at one month. Most of the patients found it necessary to apply the ointment at least once daily for continued benefit, although 3 patients were able to discontinue its use. M. Cohen.

Contact Dermatitis Due to Benzalkonium Chloride (Zephiran Chloride). Saunders, W.: New York J. Med. **53**: 2700, 1953.

Redness and edema of the upper eyelid and angular mandibular adenopathy appeared in a 10-year-old boy following the local application of an aqueous 1:1,000 solution of Zephiran Chloride. On a previous occasion, the application of a colored tincture of Zephiran to a skin scratch had resulted in an erythema which lasted for one week. Patch tests with aqueous Zephiran 1:1,000 gave positive reactions. The importance of this type of contact dermatitis is stressed because of the increasing popularity of this drug as a topical disinfectant in the treatment of common scratches and cuts. C.

Cortisone in the Treatment of Pruritus Ani. Herfort, R. A.: New York J. Med. **53**: 2871, 1953.

Five patients with long-standing pruritus ani refractory to all previous therapy were treated with oral cortisone for a period of three weeks. In three of these patients, there was associated anorectal disease which was treated surgically prior to the administration of cortisone. Both the idiopathic and secondary pruritus ani cleared completely after cortisone therapy. There was no recurrence of pruritus four to six months after cessation of the drug. C.

Otorhinology and Ophthalmology

Etiologic Analysis of One Hundred Cases of Ménière's Symptom-Complex. Gundrum, L. K.: Arch. Otolaryng. **57**: 123, 1953.

One hundred cases of Ménière's symptom-complex were analyzed from the point of view of etiology. Forty-three cases were apparently precipitated by head injury, 34 cases were associated with allergy, 10 were associated with infection, and in 13 the underlying cause of the symptom-complex could not be attributed to allergy, infection, or injury. In 28 of the 34 cases in whom the clinical picture of Ménière's symptom-complex was attributed to allergic

factors, eosinophils were observed in the postnasal secretions. The importance of the cytologic examination of the postnasal secretions was demonstrated particularly in this group. Only 12 patients (35.3 per cent) had either a personal or a familial history of allergy. Had cytologic study of postnasal secretions not been done, the cause of the symptoms in 16 (47 per cent) of this group might have been missed. Twenty-seven of these 34 patients received allergic therapy, including hyposensitization and, in 9 cases, antihistamines were administered. Among the 27 patients under allergic management, 26 were improved. Hearing tests before and after allergic treatment showed improvement in 7 of the 16 patients who had had impaired hearing prior to allergic treatment. In all 10 cases of the group in which the Ménière's symptom-complex was associated with infection, neutrophils were observed in the postnasal secretion. Treatment in this group consisted of administration of antibiotics or histamine and the use of a low sodium diet. The cytologic picture of the postnasal secretion was normal in 9 cases of Ménière's symptom-complex not associated with allergy, infection, or injury. Definite conclusions as to the etiologic significance of allergy and infection in Ménière's symptom-complex cannot be drawn from so small a series of cases. It is suggested, however, that the presence of eosinophils in the postnasal secretions strongly suggests allergy as the cause of Ménière's symptom-complex in those cases. C.

Adenotonsillectomy and Its Relation to Asthma. Sobel, G.: Ann. Allergy **11**: 583, 1953.

Three schools of thought exist with respect to the relationship between the tonsils and adenoids and bacterial allergy: 1. There are those who believe that tonsils and adenoids can act as foci of infection and that their early removal can prevent or favorably influence asthma. 2. There are others who believe that the adenoids and tonsils are important in preventing the spread of infection and should not be removed. Their removal can precipitate asthma in allergic individuals or increase the severity of an existing asthma. 3. There are some who feel that the indications for adenotonsillectomy are the same for allergic and nonallergic individuals. The removal of the tonsils and adenoids, however, cannot affect the asthmatic condition since they have no bearing on the basic allergic process.

In view of these conflicting opinions, the case histories of 100 asthmatic patients in whom infection was believed to play the dominant role were reviewed. Of the 100 patients, 68 had had adenotonsillectomy before coming under allergic management. Seven of the entire group had had more than one adenotonsillectomy performed and several had had adenoidectomies as many as four times. There were only four patients in the group on whom an adenotonsillectomy had to be performed after allergic management had been instituted.

Forty of the patients had their first attack of asthma after adenotonsillectomy. Twenty-eight per cent of these patients had their initial attack within the first year after adenotonsillectomy, 40 per cent within two years, and 54 per cent within three years after the operations. Of 28 patients who had had surgery after the onset of their asthma, 82 per cent had a recurrence within a year, 89 per cent within two years, and 100 per cent within four years.

When the patients were classified as to the severity of their asthma, there was essentially the same percentage of mild, moderate, and severe asthma in the group which had retained their tonsils and in the group in which surgery had been performed.

The indications for adenotonsillectomy in the group which developed asthma initially after the operation, were repeated sore throats, ear infections, enlarged adenoids, and recurrent colds. Eighty per cent of the cases who developed their asthma within one year of the adenotonsillectomy had been operated on because of "recurrent colds." It is probable that many of these patients had undiagnosed allergic vasomotor rhinitis. No nasal smears had been made on any of these patients. Although the month of the year in which the surgery had been performed was not accurately recorded in all of the histories, it was noted that four patients who were operated on during the ragweed pollen season immediately developed severe bronchial asthma. These findings demonstrate that the indications for adenotonsillectomy should be carefully evaluated and that attempts should be made to differentiate allergic vasomotor rhinitis from recurrent colds. Repeated nasal smears for eosinophils should be done.

It is concluded that adenotonsillectomies performed to relieve an allergic condition are usually unsuccessful and that regrowth of adenoid tissue should make one suspect the existence of allergy. F.

Intranasal Cortisone. Preliminary Study. Wall, J. W., and Shure, N.: Arch. Otolaryng. **56**: 172, 1952.

Fifty-two patients with verified allergic rhinitis and 13 patients with "so-called vasomotor rhinitis" were given a series of injections of cortisone suspension directly into the inferior turbinates. Of the 52 patients with unmistakable allergic rhinitis, 42 or 80.7 per cent obtained relief of symptoms lasting from 6 weeks to 8 months. Only one of the 13 patients with vasomotor rhinitis in whom no allergy could be demonstrated was benefited.

Of the allergic patients, 5 with acute allergic rhinitis experienced immediate and dramatic relief. Of 6 patients with chronic perennial allergic rhinitis associated with asthma, 5 responded well to this form of therapy. Of 5 patients with chronic allergic rhinitis with nasal polyps, 4 were symptomatically relieved, although the size of the polyps was not affected. Of 36 patients with uncomplicated chronic nasal allergy, 28 were benefited.

This procedure is advocated for prolonged symptomatic relief of allergic rhinitis, especially of the seasonal variety. C.

Clinical Evaluation of Aramine. A New Sympathomimetic Amine. Taylor, G. W.: Arch. Otolaryng. **56**: 213, 1952.

Aramine Hydrogen Tartrate was either sprayed or instilled into the nose of 200 patients with a variety of nasal conditions. This drug, levo-l-(m-hydroxyphenyl)-2-amino-l-propanol d-hydrogen tartrate, is a new sympathomimetic amine which was found to be isotonic, and slightly acid (pH 6.0) buffered. It is an effective vasoconstrictor without vasodilatory action and without local or systemic toxicity. Used in 0.25 per cent solution in a group of 24 patients with nasal allergy, some vasodilation was noted after the drug had been used for 48 to 72 hours. In no case was there any evidence of damage to the nasal mucosa from prolonged use. C.

Miscellaneous

The Incidence of Allergy to Drugs in Pediatric Practice. Berkowitz, M., Glaser, J., and Johnstone, D. E.: Ann. Allergy **11**: 561, 1953.

The frequency with which various drugs are used and the incidence of reactions to them was investigated in a group of 500 unselected children seen

in the private practice of a pediatric allergist and in an outpatient pediatric clinic. Sixty-six per cent of these children had a history of allergic diseases. Reactions regarded as allergic were noted in 20 per cent of the allergic children as against 2.4 per cent in the nonallergic group. "Side reactions" to the drugs occurred in 36 per cent of the allergic children as compared to 3.5 per cent of the nonallergic children. A history of a reaction was obtained in 10 per cent of allergic children who had received penicillin, but no such reactions were noted in nonallergic children who had had penicillin. A total of 411 of the group had received penicillin. Aureomycin and Terramycin gave reactions in 3.7 per cent and 3.4 per cent, respectively, in the allergic group, but no reactions were observed with these drugs in the nonallergic group. The incidence of reactions from the sulfonamides was 6.7 per cent in allergics and 4.7 per cent in nonallergics. Benadryl and Pyribenzamine were found to be the cause of allergic reactions in 2.3 per cent and 1.7 per cent, respectively, of the allergic children. Other antihistaminics were not offenders. Aspirin, which was administered to 450 of the 500 children, gave reactions in 1.9 per cent of the allergics and no reactions in the nonallergics. These studies indicate that a much higher incidence of allergic reactions and side reactions occurs in allergic children than in nonallergics. It is suggested that many of the so-called side reactions to drugs may actually be minor allergic reactions. F.

Hypersensitivity to Bee Sting. Report of Fatal Case and Review of Literature. Schenken, J. R., Tamisiea, J., and Winter, F. D.: Am. J. Clin. Path. **23**: 1216, 1953.

The authors state that theirs is the tenth report of autopsy findings in fatal allergic reactions to bee sting. The patient, a man, had had violent reactions including cramps, diarrhea, and vomiting following bee stings at the age of 18 and again at the age of 20. When he was 21, he was stung on the temple by a bee, became immediately nauseated, weak, cold, developed abdominal cramps, frothed at the mouth, became cyanotic, and developed convulsions. He was pronounced dead twenty-five minutes after being stung. Necropsy showed dilatation of the right atrium and right ventricle of the heart to double normal size, thick tenacious mucus in addition to frothy fluid in the bronchi, bronchioles, and trachea, marked edema of the vocal cords and epiglottal folds, and edema of the cerebral convolutions of the brain. The other organs were normal. The autopsy findings of the other nine reported cases are summarized. K.

Serum Neuritis: 20 Cases Following Use of Antitetanic Serum. Garvey, J. L.: Postgrad. Med. **13**: 211, 1953.

Twenty cases of neuritis were observed following the administration of tetanus antitoxin. The ages of the patients ranged from 18 to 61 years. Eighteen were men and 2 were women. Eight had symptoms of severe serum sickness, 10 cases were moderately severe and 2 were mild. In 6 patients, the neuritis was generalized; in 5, it was localized to the right shoulder; and in 3, it was limited to the left shoulder. It was present in both shoulders in 2 cases, over the musculospiral nerve in 2, and in the ulnar nerve in one. In 2 cases, there were associated cerebral manifestations. Neuritis should be suspected in serum sickness, if severe localized or radicular pain appears early in the course. Usually the pain is so severe that the detection of paralysis is difficult. Flaccid atrophic paralysis occurs in the neural segments where the

pain is distributed. Although the pathogenesis of the disease is still unknown, it is suggested that it is due to urticarial edema of the perineural tissue with the consequent production of compression neuropathy. E. W.

Anaphylaxis

Anaphylactic Shock in the Mouse Vaccinated With Hemophilus Pertussis. Malkiel, S., Hargis, B. J., and Feinberg, S. M.: J. Immunol. **71**: 311, 1953.

Female albino mice of the Swiss-Webster strain were sensitized by the intraperitoneal inoculation of crystalline egg albumin (Ea) or bovine serum, mixed with Hemophilus pertussis phase I organisms. The addition of the pertussis organisms markedly enhanced the sensitivity of the mice to intravenous challenge with the antigen. A group of such mice showed a 74 per cent mortality after challenge with Ea, whereas a control group sensitized with Ea alone had a 5 per cent mortality. The same amount of Ea, when incorporated in Freund's adjuvant, was slower and considerably less effective in producing sensitization. A high degree of anaphylactic sensitization was attained with various fractions of the pertussis organisms, such as an acellular saline extract of defatted organisms, an alcohol-precipitated antigen, and the supernate from sonically disintegrated organisms. Effective sensitization resulted when the antigen was given intravenously and pertussis intraperitoneally on the same day. It was inferred from these findings that the enhancement of antigenicity was not mediated by virtue of the adjuvant or "schlepper" effect of the pertussis cells.

Immunologic studies failed to detect precipitating or nonprecipitating antibodies in mouse anti-Ea serum. In neither pertussis inoculated nor control mice could passive transfer with homologous "antisera" be effected. It was suggested that tissue or sessile antibodies may be responsible for the heightened sensitivity. M. Cohen.

Quantitative Studies on Anaphylaxis, Deallergization, and Desensitization. Baserga, R., and Bergamini, F.: J. Immunol. **71**: 397, 1953.

Guinea pigs were given two injections, 5 days apart of egg albumin combined with Freund's adjuvant. After 30 days, some of the animals were bled and the serum examined for antibody content, while others were challenged intravenously with a sublethal shocking dose of egg albumin and bled 2 days later. All animals in the latter group showed severe nonfatal anaphylactic shock, which was accompanied by a marked drop in the titer of precipitins and in the amount of antibody-N in their sera as compared with the sera of the unchallenged controls. When a lethal dose of antigen was given intravenously 48 hours after the sublethal dose, only mild symptoms of anaphylactic shock developed. This was regarded as evidence that the guinea pigs had been deallergized by the sublethal dose.

Guinea pigs which were repeatedly injected with egg albumin without adjuvants showed very low titers of precipitins and no detectable antibody-N in their sera. Despite their low antibody titers, these animals required much less antigen to produce shock than did the animals sensitized with the aid of adjuvants. Therefore, it was concluded that the quantitative changes in the antibody content of the serum did not account for the refractory states to anaphylaxis in the above experiments. The refractory states in anaphylaxis were attributed to nonspecific changes in the reactivity of the animals. M. Cohen.

Anaphylaxis in the Mouse Produced With Crystalline Bovine Albumin. Solotorovsky, M., and Winsten, S.: J. Immunol. **71**: 296, 1953.

White mice were injected subcutaneously at 4-day intervals with 1 mg. of crystalline bovine albumin dissolved in saline. After 8 sensitizing doses followed by a 4-week rest period, a group of mice was challenged by the intravenous injection of 1 mg. of bovine albumin. Approximately one-third of the animals died in anaphylactic shock. When the number of sensitizing injections was increased to 16, approximately two-thirds of the mice succumbed after challenge. The antigenicity of the bovine albumin was enhanced by alum-precipitation. Since a satisfactory degree of susceptibility to anaphylactic shock was demonstrated, it was suggested that the mouse be considered a favorable test animal for the investigation of anaphylaxis.
M. Cohen.

Pharmacology, Physiology, and Pathology

Immunologic Mechanism of Leukocyte Abnormalities. Finch, S. C., Ross, J. F., and Ebaugh, F. G., Jr.: J. Lab. & Clin. Med. **42**: 555, 1953.

Leukocytic antisera were prepared by injecting rabbits subcutaneously with mixtures of adjuvants and leukocytes taken from patients with chronic lymphocytic or granulocytic leukemias. These injections were given once weekly for 3 weeks. Five weeks after the initial injection, each animal was injected subcutaneously with saline-washed leukocytes from the same patient. In the sixth week, the rabbits were bled and the antisera prepared. In vitro cytologic studies, in which the leukocytic antisera were incubated with plasma-leukocyte suspension from normal subjects, revealed three striking morphologic features: (1) clumping of granulocytes resembling the "rosettes" of the L. E. test; (2) phagocytosis of granulocytes in some cases producing cells with an appearance indistinguishable from Hargrave's L. E. cells; (3) vacuolization of neutrophilic granulocytes and monocytes. Agglutination studies by either the sedimentation or tube agglutination techniques indicated that the antigranulocytic serum produced marked agglutination of leukemic granulocytes but not lymphocytes, while the antilymphocytic serum had a very limited capacity to promote agglutination of either human leukemic granulocytes or lymphocytes. The ability of both antigranulocytic and antilymphocytic sera to produce these effects, namely, leukophagocytosis, leukoagglutination and lytic changes, was markedly reduced or completely destroyed following absorption with granulocytic leukocytes, but remained unchanged following absorption with lymphocytes. Leukophagocytic activity was not reduced by heating the sera to 56° C. for 30 minutes; the reaction did not occur below 10° C. or above 40° C., but proceeded rapidly at room temperature over a pH range of 7 to 8. It is suggested that the "L. E." factor may be closely related to the leukocyte antibody. The action of the leukocyte antibody clearly demonstrates three mechanisms by which leukocytes may be removed from the circulation should leukocytic autoimmunization occur. E. W.

The Inhibition of the Local Shwartzman Reaction by Heparin. Cluff, L. E., and Berthrong, M.: Bull. Johns Hopkins Hosp. **92**: 353, 1953.

Skin sites were prepared in rabbits by the intracutaneous injection of either the P-25 polysaccharide of *Serratia marcescens* or a meningococcal filtrate. In the experimental animals, heparin was injected in 5 mg. doses every 30 to 45 minutes, starting 5 to 15 minutes prior to the provocative intravenous dose of toxin and continuing for at least 4 hours thereafter. The control animals

were not given heparin but were otherwise similarly treated. The Shwartzman reaction was considered positive only if gross hemorrhage plus necrosis and sloughing occurred. Heparin almost completely blocked the Shwartzman reaction; a few small hemorrhages occurred but these disappeared within 24 or 48 hours and no necrosis or sloughing was observed. The toxic or febrile reaction produced by the toxins was not affected by the heparin. There was a suggestion that the tendency toward leukopenia was less pronounced in the treated animals. Systemic hemorrhagic signs did not appear in the heparinized rabbits dying after the toxin administration. Ecchymosis around venipuncture sites was the only hemorrhagic manifestation noted. It is suggested that thrombus formation rather than hemorrhage through damaged vascular walls is the fundamental process producing the Shwartzman reaction. R. W.

The Effect of Bacterial Pyrogen Upon the Experimental Cardiovascular and Renal Lesions of Anaphylactic Hypersensitivity. Bennett, I. L., Guzi, L. B., and Roberts, E.: J. Lab. & Clin. Med. **41**: 559, 1953.

Each of 60 rabbits was given an intravenous injection of horse serum in a dose of 10 ml. per kilogram of body weight. Immediately thereafter, 30 animals received an intravenous injection of 2.0 ml. of a suspension containing 50 mg. per milliliter of Piromen, a concentrate of pyrogenic material from a Pseudomonas species. Control animals received similar amounts of pyrogen-free saline solution. Daily injections of pyrogen or saline were continued for 14 days. Fifteen days following the sensitizing injection of horse serum, all animals were given 0.1 ml. of undiluted horse serum intradermally. Skin reactions were examined and measured on the fifteenth day, immediately before the animals were sacrificed. Blood was taken at three-day intervals for precipitin studies throughout the experiment. The incidence of cardiovascular lesions, endocarditis, periarteritis and renal lesions (acute glomerulonephritis) was almost identical in both the treated and the untreated groups. Serum antibody titrations and skin test responses (Arthus reactions) revealed no essential differences in the two groups. Animals given Piromen showed no evidence of adrenal hypertrophy, thymic atrophy, or inhibition of "acute splenic tumor" which has been observed in animals treated with ACTH or cortisone. Pyrogen-treated animals showed no depletion of cortical lipoid. It was concluded that, in the dosage used in this study, Piromen exerted no significant adrenocortical stimulatory effect. E. W.

Influence of Adrenocortical Stimulation on Antibody Production. van der Slikke, L. B., and Keuning, F. J.: J. Lab. & Clin. Med. **42**: 389, 1953.

Rabbits that had received three weekly intravenous injections of paratyphoid vaccine rich in H-antigen were given a single injection of ACTH (10 mg.) 9 days or 6 months later. H-agglutination titers were then determined at varying periods of time up to 24 hours after the administration of ACTH. It was found that during the first 24 hours following the administration of a single dose of ACTH, there was a tendency for the serum-agglutinin titers to fall. In another group of experiments, animals which had been similarly prepared with paratyphoid vaccine received a single injection of ACTH, 20 days after the last antigen administration. A control group received saline at the same time. Twenty-four hours later both groups were sacrificed and tissue cultures were prepared from the red and white splenic pulp. The spleens of rabbits treated with ACTH produced about twice as much antibody as the controls. The histologic picture of the spleens is described. E. W.

Cortisone Effect on Antibody Levels in Rabbits Simultaneously Immunized With Serum Albumin and Sheep Cells. Hanan, R., and Overman, J. R.: Proc. Soc. Exper. Biol. & Med. **84**: 420, 1953.

Rabbits were injected simultaneously with bovine serum albumin and sheep red cells over a 15-day period. Cortisone was given to one-half of the animals, starting 3 days prior to immunization and continuing until the animals were bled on the seventh day after the last injection. Quantitative precipitin tests were done to measure anti-albumin N. Hemolysin and hemagglutinin were titrated by serum dilution and determinations of agglutinin N. The results were compared to those of untreated controls. Cortisone seemed to suppress the formation of antibody to bovine serum albumin but had little or no effect on the production of hemolysin or agglutinin. M. Cohen.

Inactivation of Histamine by Lung Tissue From Histamine-Sensitive and Histamine-Resistant Mice. Kind, L. S., and Woods, E. F.: Proc. Soc. Exper. Biol. & Med. **84**: 601, 1953.

Mice were made sensitive to histamine by repeated inoculations of H. pertussis vaccine. The lungs of 5 of these animals were pooled and ground. To this material, a weighed amount of histamine per gram of lung tissue was added. The mixture was then incubated overnight and assayed biologically for its remaining histamine content. As a control, the lungs of uninoculated, histamine-resistant mice were used in similar experiments.

The lung tissue from uninoculated controls inactivated approximately 3 times as much histamine as did the lung tissue from pertussis-inoculated mice. Since the lung tissue from pertussis-inoculated mice showed a reduced ability to destroy histamine, it was suggested as an explanation for the increased sensitivity of these animals to histamine. M. Cohen.

The Effect of Antibiotics Upon the Immune Response. Kingsley, K. M.: J. Immunol. **71**: 119, 1953.

The effect of several antibiotics upon the primary immune response in rabbits was studied. Small amounts of iodinated bovine gamma globulin were injected intravenously into rabbits who were maintained on Aureomycin, Terramycin, dihydrostreptomycin or penicillin throughout the experimental period. The antibiotics were given subcutaneously and in doses comparable to those used clinically in man. Samples of blood were taken 15 minutes after the immunizing injection and daily thereafter for 10 days and counted for radioactivity with a Geiger-Müller tube. The rate of loss of radioactively labeled antigen served as a measure of the immune response.

Approximately one-half of the animals under antibiotic treatment showed greater retention of antigen than controls, indicating a depression of their immune response. Extensive statistical studies were utilized in interpreting the experimental data obtained. M. Cohen.

The Effect of Antigen Administration on the Behavior of I^{131} Labeled Rabbit Anti-ovalbumin in Mice. Masouredis, S. P., Melcher, L. R., and Shimkin, M. B.: J. Immunol. **71**: 268, 1953.

I^{131} labeled rabbit anti-ovalbumin was administered intravenously in mice, and 23 hours later ovalbumin was injected intraperitoneally. Control animals received only the I^{131} antibody. The fate of the I^{131} antibody in each instance was determined by a metabolic balance study of I^{131} in which interval determinations of plasma and daily determinations of excreta radioactivity were made with a Geiger-Müller tube.

Following injection of the antigen, a precipitous drop in plasma I^{131} occurred over a 4-hour period. This drop greatly exceeded the rate of loss of antibody in the controls. Following this, the plasma I^{131} decreased at a rate similar to that of the controls. The remaining circulating radioactivity was due chiefly to labeled nonantibody globulin, which suggested that all the reacting antibody in the globulin injected had been removed from the plasma within a few hours after the antigen was administered.

A further manifestation of an in vivo I^{131} antibody-antigen reaction was evidenced by the significantly greater excretion of I^{131} in mice during the 48-hour period following injection of the specific antigen than occurred in the control animals. M. Cohen.

The Effect of Rabbit Antibody Administration on the Behavior of I^{131} Labeled Human Serum Albumin in Mice. Melcher, L. R., Masouredis, S. P., and Shimkin, M. B.: J. Immunol. **71**: 275, 1953.

Mice were injected intravenously with I^{131} labeled human serum albumin (HSA) and 24 hours later intraperitoneally with rabbit anti-HSA. The fate of the I^{131} antigen was determined by a metabolic balance study in which determinations of radioactivity in the plasma and excreta were made at intervals with a Geiger-Müller tube.

After administration of the specific antibody, there was a rapid removal of I^{131} from the plasma associated with transient pooling of the radioactivity in the liver and spleen. This was followed by release and excretion of the radioactivity associated with the labeled antigen within 48 hours. The distribution and behavior of I^{131} duplicated that found in mice which were injected first with labeled antibody and then with the related antigen. It was suggested that an in vivo antigen-antibody reaction is manifested by changes in tissue, excreta, and plasma I^{131} levels that are identical regardless of the component which carries the I^{131} label. M. Cohen.

The Histology of Antigenically Stimulated Lymph Nodes in Rabbits Given ACTH or Cortisone. Craig, J. M.: Am. J. Path. **28**: 629, 1952.

Rabbits were given a single injection of typhoid 0 antigen and then were treated daily with ACTH or cortisone until they were sacrificed 48 hours, 96 hours, or 8 days later. The usual antigenic stimulation of the regional lymph nodes, as seen in the controls, was depressed in the treated animals. This repressive influence wa noted histologically in the reduced mas of the affected lymph nodes, in their narrowed cortex, in their lack of reaction centers, and in the partial inhibition of the formation of germinal centers and mitotic figures.

The antibody titers in the hormone-treated animals and in the control animals showed no significant variation. J. S.

Agranulocytosis During Isoniazid Therapy. Varadi, S., and Kelleher, T. D.: Lancet **1**: 145, 1953.

A 20-year-old diabetic with tuberculosis was treated with streptomycin, p-aminosalicylic acid and isoniazid. Twenty-two days following cessation of the streptomycin therapy but while still on treatment with the other two drugs, he developed fever, hepatomegaly, and mild jaundice. A blood count showed agranulocytosis (4,200) with maturation arrest at the promyelocyte level as demonstrated by sternal marrow puncture. The patient was treated with penicillin, pyridoxine, Aureomycin, and methionine. The temperature fell by lysis and six days after discontinuing p-aminosalicylic acid

and isoniazid therapy, granulocytes began to form and the temperature was normal. Within three weeks, the white blood count was completely normal after having fallen to a level of 1,700 on the fifth day of the reaction. The hemoglobin level, red cells, reticulocytes, and platelets were not affected during the hematologic reaction. The authors stress the need for careful hematologic follow-up on all patients receiving isoniazid therapy. R. W.

Diphenhydramine (Benadryl) and Tripelennamine (Pyribenzamine) Intoxication in Children. Judge, D. J., and Dumars, K. W., Jr.: Am. J. Dis. Child. **85**: 545, 1953.

The authors discuss the pharmacology and review the literature on Pyribenzamine and Benadryl reactions. Two cases of toxicity from overdoses of antihistamines are reported. The first patient was a 2-year-old youngster who swallowed 500 mg. of Benadryl and became very excited. She developed hallucinations, muscle twitching, hyperreflexia, and intermittent tremors. These symptoms gradually subsided following gastric lavage, sedatives, and parenteral fluid administrations. Within 48 hours, the reaction had completely terminated. The second patient was a 2-year-old girl who had swallowed 100 mg. of Pyribenzamine. She became very weak, lethargic, and showed a horizontal nystagmus. After several days of severe drowsiness, the patient gradually responded to stimulants and symptomatic therapy. The authors stress the marked variation in symptoms that may occur from an overdose of antihistamines. Severe reactions in youngsters usually produce some form of central nervous system involvement. They urge that more caution be exercised in prescribing antihistamines, especially when there is no clear-cut indication for using these drugs. R. W.

Attempts on Passive Local Sensitization by Intracutaneous Injection of Cells From Freshly Excised Lymph Nodes of Eczema Allergics. Haxthausen, H.: J. Invest. Dermat. **21**: 237, 1953.

Suspensions of lymphocytes were obtained from lymph nodes excised from each of 8 eczematous patients allergic to various chemical compounds. To preserve the viability of the lymphocytes, 0.05 c.c. of each suspension was injected intracutaneously into normal subjects within 30 minutes after extirpation of the node. Control sites were made with a portion of the suspension which had been frozen and thawed in order to kill the lymphocytes. Within 48 hours, patch and intracutaneous tests with the specific antigen were performed and read 24 hours later. At the time of testing, slightly larger papular infiltrations were noted at the living lymphocyte sites than on the control sites.

The patch tests gave consistently negative results in all cases. The intracutaneous tests produced slight reactions which were definitely more pronounced on living lymphocyte sites than on the control sites in 5 of the 8 different transfers. Because of the induration present at the sensitized sites at the time of testing, it was felt that the estimates of the intracutaneous reactions could not be relied upon. For this reason, it was concluded that the positive results obtained could not be considered as absolute proof that passive sensitization had been induced. M. Cohen.

Allergic Granulomatosis Associated With Visceral Larva Migrans. Case Report With Autopsy Findings of Toxocara Infection in a Child. Brill, R., Chung, J., and Beaver, P. C.: Am. J. Clin. Path. **23**: 1208, 1953.

A 2-year-old male child of Italian ancestry gave a history of being "less active than usual" for 2 weeks prior to hospitalization and had run a low-

grade fever for the first 3 days of this illness. On admission, the temperature was 37.8° C., the pulse rate was 140 per minute and the respirations were 54 per minute. A short systolic heart murmur was heard over the entire precordium and the liver was felt 3 cm. below the right costal margin. Urinalysis showed 4-plus albumin, a specific gravity of 1.032, and a strongly positive hemoglobin test. Occasional red and white blood cells were present and a few granular casts. The red blood count was 4.7 million per c.mm., and the white blood cell count was 31,400 with 40 per cent eosinophils. X-ray showed peribronchial infiltration of the left upper lung field but no consolidation. The tuberculosis patch test gave a negative reaction. The child developed cyanosis and lethargy and died on the third hospital day. Necropsy revealed disseminated visceral granulomatous lesions, often in relation to "a severely altered small vein," in the heart, kidneys, liver, and lungs. One pulmonary nodule contained a Toxocara larva. Extensive degeneration and inflammatory changes were noted in the diaphragm and in the striated muscles. Toxocara is the larval form of cat or dog Ascaris which, instead of maturing in an abnormal host, remains in the larval stage and migrates in the viscera. This child frequently played with cats and was a known dirt eater. It is speculated that death was due either to an antigen-antibody reaction or to a direct effect of the toxic antigen, with the extensive degeneration of the diaphragm and other respiratory muscles playing a major role in his terminal respiratory failure. K.

The Transfer of Experimental Allergic Encephalomyelitis in the Rat by Means of Parabiosis. Lipton, M. M., and Freund, J.: J. Immunol. **71**: 380, 1953.

Rats were given intracutaneous injections of a guinea pig spinal cord emulsion combined with adjuvants. Seven or more days later, these rats were joined in parabiosis with normal rats as recipients. Parabiosis was established by cutting through the abdominal walls and sewing them so as to form a common peritoneal cavity. Pairs of animals were killed after 7 to 12 days of parabiosis and histological examinations of the central nervous system of the rats were made. Encephalomyelitis was present in 12 donors and 5 recipients of 40 such rats. Since the parabiotic rats were sacrificed before active sensitization was demonstrated to occur in the control animals, it seemed likely that passive sensitization had occurred in the parabiotic recipients. Whether the transfer of encephalitis was effected by serum antibodies or white blood cells or some other agent could not be determined. However, the failure of pregnant guinea pigs with encephalomyelitis to transmit the disease to their fetuses was considered evidence against the role of serum antibodies.

M. Cohen.

Relative Failure of Oral Cortisone in Erythema Nodosum. Pike, J. B., and Elder, M. J.: New York J. Med. **53**: 2694, 1953.

A 36-year-old white woman with typical lesions of erythema nodosum was treated with cortisone orally for from 4 to 6 days. The lesions cleared promptly within 3 or 4 days, but, on 3 successive occasions, recurred soon after the drug was discontinued. When a relapse occurred for the fourth time, maintenance dosage was continued for 6 weeks and recovery was complete. A total of 3,325 mg. of cortisone was required before the condition finally cleared. This is in contrast with one of the previously reported cases which required only 275 mg. for recovery. It is emphasized that cortisone merely acts as a suppressive agent and that erythema nodosum is a self-limited disease. The sedimentation rate is the best index of the basic recovery of the patient. C.

A Study of Antibody Formation in Patients With Malignant Lymphomas. Geller, W.: J. Lab. & Clin. Med. **42**: 232, 1953.

Twenty-four patients with either lymphosarcoma or Hodgkin's disease and 16 normal individuals with no known malignant disease received 0.1 mg. of type-specific pneumococcal capsular polysaccharide I (S_1) subcutaneously. Of the 24 patients, 14 were in good health with no signs of active disease and 10 were hospitalized with active disease. The hospitalized group was initially treated with nitrogen mustard one to two days prior to the injection of type-specific polysaccharide and some of these patients also received local irradiation, steroids, or triethylene melamine before completion of the study. Two and six weeks after the injection of type-specific polysaccharide, quantitative determinations of antibody titers to S_1 were made on the blood of all subjects. Sixty-two per cent of the control group showed significant titers to S_1. Of the patients with malignant lymphomas, only 14 per cent of those with inactive disease and 20 per cent with active but treated disease showed significant antibody titers. No conclusions could be drawn as to the effect of nitrogen mustard on antibody formation in these patients. These results confirmed the concept of the poverty of antibody response in patients with malignant lymphoma. E. W.

The Response to Antimicrobial Therapy of Anergic and Partially Anergic Patients. I. Changes in the Tuberculin Sensitivity of Individual Patients. Woodruff, C. E., Steininger, W. J., Kelly, R. G., and Kreisel, H.: Am. Rev. Tubere. **67**: 286, 1953.

All patients admitted to a tuberculosis sanatorium were routinely skin tested with 0.1 ml. of a 1:10,000 dilution of old tuberculin by the intracutaneous technique. A reaction was considered positive when an area of induration 5 mm. or more in diameter developed at the test site within 48 hours. Patients who failed to react to the 1:10,000 dilution were retested at 48-hour intervals with a 1:1,000 dilution of old tuberculin. The final dilution used was 1:10 old tuberculin. A group of 36 patients whose sputum was positive for tubercle bacilli failed to react to the first two dilutions of tuberculin. These patients were started on streptomycin therapy and retested with tuberculin at frequent intervals. Of the 36 anergic patients, all except 2 showed an eventual increase in sensitivity to the 1:10,000 level and an improvement in their tuberculosis. The 2 who remained anergic died within a few months. Increased sensitivity to tuberculin in patients of this type frequently preceded roentgenographic evidence of improvement. E. W.

A Cutaneous Test for Rheumatic Activity in Children. Streitfeld, M. M., and Saslaw, M. S.: Proc. Soc. Exper. Biol. & Med. **84**: 628, 1953.

The cutaneous response to the inunction of 5 per cent tetrahydrofurfuryl ester of nicotinic acid (Trafuril) was studied in 337 children, some of whom had active rheumatic fever. Normal subjects and patients with nonrheumatic conditions reacted to the inunction with localized hyperemia or edema. Of 22 patients with active rheumatic fever, 20 failed to show this typical response. Rheumatic fever patients whose active symptoms were being suppressed by cortisone or aminopyrine responded in the normal manner. An atypical response was also observed in individuals with streptococcal sore throat. It was suggested that this test may prove useful in evaluating the activity status of rheumatic patients. The mechanism of the reaction is being investigated. M. Cohen.

The Use of Delayed Films in Bronchography. Abrams, H. L., Hencky, G., and Kaplan, H. S.: Radiology **61**: 317, 1953.

Bronchograms taken in the usual manner are at times unsatisfactory because of incomplete visualization of some of the major or segmental bronchi. In 100 consecutive bronchograms performed on 75 patients, delayed films were taken from 30 to 60 minutes after the initial films. During the interval, coughing and other normal activity was permitted. In 42 of the 100 cases, there was complete filling of all lobes and delayed films were superfluous. In 36 cases, delayed films proved of definite value. In 10 of the 36, a diagnosis of bronchiectasis was established, although it was not demonstrable in the original study. In 13 cases, bronchiectasis was excluded, although the original films were highly suggestive of this diagnosis. In the remaining 13 cases, bronchi not previouly filled were delineated. There were 22 instances in which both the original films and the delayed films were unsatisfactory. Delayed films were of value in outlining the lower lobes, the right middle lobe, and the lingula of the left upper lobe. They were of little or no value in studying the upper lobes.

It was concluded that delayed films may prove useful in overcoming the failure of adequate filling of branch bronchi and should be taken whenever the bronchi to the lower or middle lobes are inadequately demonstrated.

J. S.

A New Technique for Bronchography: Lipiodal Vaporization. Girard, J., Grilliat, J. P., and Faucompre, P.: Presse méd. **61**: 914, 1953.

A new technique for bronchography is described. The patient is prepared by postural drainage. He receives 0.2 Gm. Gardenal and 0.75 mg. atropine. Local anesthesia is induced with 0.5 per cent Pontocaine. A special double tube is introduced into the trachea to the level of the aortic arch. A mixture of one-third heavy Lipiodal 40 per cent and two-thirds Lipiodal "F" 40 per cent is employed. Six c.c. of the mixture vaporized into the end of the tube for 90 seconds impregnates the entire bronchial tree. The method is simple and rapid. The small quantity of contrast medium employed is quickly eliminated and limits the toxic effects of the iodine.

I. Glazer.